REMARKS

Entry of the foregoing, examination and further and favorable consideration of the subject application in light of the following election **with traverse** are respectfully requested.

Amendments

The Office Action indicates that claim 18 was missing in the instant application as filed. Claims originally numbered 19-48 have been renumbered 18-47 by the Examiner to eliminate the missing claim number.

By the present amendment, a clean version of the entire set of pending claims is submitted for the convenience of the Examiner pursuant to 37 C.F.R. § 1.121(c)(3). The clean version of the entire set of pending claims reflects the renumbering of original Claims 19-48 to Claims 18-47. Renumbered claims 19, 21, 22, 23, 25, 28, 31, 32, 34, 35, 37, 38, 40-44 and 46-47 have been amended to reflect the appropriate renumbering of dependencies. Claim 2 has also been amended to correct a typographical error. Claim 2 now depends from Claim 1 as intended rather than depending on itself.

No prohibited new matter is believed to have been introduced by way of the above amendments.

Election with Traverse

Applicants hereby elect, with traverse, **Group I (Claims 1, 2, 6, and 7)** and further elect the species of "a protein" in Claim 7. Applicants hereby traverse the restriction

requirement because it would not impose an undue burden upon the Examiner to search and examine all the claims of the application together. In particular, it would not impose an undue burden upon the Examiner to examine the screening methods of Groups II-VII, XIII and XIV concurrently with Group I. Therefore, Applicants request reconsideration of the restriction requirement and that these groups be rejoined and examined together.

For a restriction requirement to be proper, there **must be a serious burden** upon the examiner if restriction is not required. MPEP § 803. If the search and examination of an entire application can be made without **serious burden**, the examiner **must** examine it on the merits, even though it includes claims to independent or distinct inventions. *Id.* (emphasis added). The present restriction requirement is improper because the claims have been clearly overly restricted into unreasonably small groups in violation of the policy of the U.S. Patent and Trademark Office set forth in the MPEP at § 803. On page 7 of the Official Action it is asserted that categorization in different classifications is evidence that the methods of the groups have acquired a separate status in the art. However, separate classification is not an independent basis for a valid restriction. The Examiner has asserted that the restricted claims are distinct, however the Official Action has not shown, or even explicitly asserted, that a serious burden would be placed upon the Examiner if restriction to the extent proposed in the Official Action is not required. For example, since there is substantial common subject matter in the claims of Groups I - VII, XIII and XIV, there would be substantial overlap in the search and examination of Groups I - VII, XIII and XIV and no serious burden would result if at least these groups were examined together. More

particularly, Applicants request that at least Groups I, II, VI be rejoined and examined together.

Moreover, the Official Action imposes a number of improper restrictions within claims, such as claims 7, 9, 12, and 14. These restrictions are improper because there is no reason to believe, or presented in the Official Action, that examination of these claims, as presented, would impose a serious burden on the Examiner. If the members of a Markush group are sufficiently few in number or so closely related that a search and examination of an entire claim **can be made without serious burden**, the examiner **must examine** all the members of the group in the claim on the merits even though they are directed to independent and distinct inventions. MPEP 803.02. Claim 7 recites a Markush-type group of only three alternative biomolecule types which may be identified in the claimed method. Claim 12 recites the two alternatives of inhibiting or enhancing activity. Claim 14 recites three alternative host systems. Surely, these are sufficiently few in number that a search and examination of the entire claims **can be made without serious burden**. Applicants request reconsideration and withdrawal of all the restrictions imposed within claims.

The lack of serious burden in concurrently examining claims of at least Groups I - VII, XIII and XIV may be clearly seen from the following considerations. The screening methods of Groups I-VII relate to the identification of a molecule which is involved in lipid regulation by assessing the interactions between the molecule in question and Zmax1 (including certain tabulated polymorphisms) or HBM nucleic acid sequences or Zmax1 or HBM. Groups XIII and XIV are directed to diagnostic methods and a diagnostic assay

which relate to the experimental observation of binding to the HBM nucleic acid sequence or to Zmax1 and HBM. The claims of each of these groups share common subject matter relating to molecular interactions with HBM and Zmax1 and nucleic acids sequences thereof and therefore the search for each of these groups will substantially overlap. The degree of overlap in the search and examination is evidence that concurrent examination of these groups would not impose an undue burden upon the Examiner.

In particular, Applicants request that Groups I, II, VI be rejoined and examined together. Groups I and VI are drawn to methods relating to identifying a molecule that binds to or inhibits the binding of another molecule to HBM or Zmax1 or differentially binds or inhibits another molecule from binding the Zmax1, or certain polymorphisms, and HBM nucleic acid sequences. The search of the subject matter of Groups I and IV are therefore nearly coextensive and there will be no undue burden upon the Examiner if Group VI is examined concurrently with Group I. Furthermore, Claim 3 (of Group II) is drawn to a method according to Claim 2 (of Group I) which includes the step of producing an antibody to the protein identified by the method of Claim 1. The Examination of Group II substantially overlaps with the examination of Group I and there will be no undue burden upon the Examiner if Claim 3 is examined concurrently with Claim 2 from which it depends.

Applicants further request that the division of species within Claim 7 be withdrawn. Claim 7 recites three preferred species of molecules which may be identified in the method of Claim 6. A thorough search of the subject matter of Claim 6 should be nearly co-extensive with the search of Claim 7 because the steps of Claim 6 are the same whether

applied to any of the species of Claim 7. Certainly, the examination of only three species of Claim 7 would not impose an undue burden on the Examiner.

Applicants further request that if Group IV is rejoined with Group I, then the species restriction within Claim 9 is reconsidered. Claim 9 recites species of subjects of the method of Claim 8. A thorough search of the subject matter of Claim 8 should be nearly co-extensive with the search of Claim 9. Therefore, the concurrent examination of the species of Claim 9 would not impose an undue burden on the Examiner.

Applicants further request that if Group VI is rejoined with Group I, then the species restriction within Claim 12 is reconsidered. Claim 12 recites alternative effects of the molecule identified by the method of Claim 11. Therefore, a thorough search of the subject matter of Claim 11 should be nearly co-extensive with the search of Claim 12. Accordingly, the concurrent examination of the alternatives of Claim 12 would not impose an undue burden on the Examiner.

With respect to Groups VIII-XII and XV-XIX, Applicants submit that the embodiments of the invention of recited in these claims are related by overlapping subject matter and that, in various combinations, these methods can be used together. As a first example, consider the methods of Group XV, directed to methods of expressing the HBM protein in tissue. One of skill in the art will appreciate that such a method may be used in conjunction with, for example, the screening methods of Groups III, IV, VII. If any of Groups III, IV, VII are rejoined with Group I and examined, Applicants also request the rejoining of Group XV therewith. Applicants submit that in view of the overlapping search

requirements of all the claims of the present application, the present restriction requirement is improper under MPEP § 803 and should be reconsidered.

In view of the foregoing, reconsideration of the restriction requirement is respectfully requested. In particular, Applicants request rejoining of Groups II-VII, XIII and XIV with Group I. At the least, Applicants request rejoining of Groups I, II, VI and the withdrawal of the restriction among the species recited in Claim 7.

Further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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Attachment to Amendment dated March 22, 2002

Marked-up Claims

2. (Amended) The method of claim [2]1, wherein said molecule is a protein.

19. (Amended) The method of claim [19]18, wherein the animal is livestock, primates, humans, canines, felines, rodents, birds, reptiles, fish, or amphibians.

21. (Amended) The method of claim [21]20, wherein the patient is livestock, primates, humans, canines, felines, rodents, birds, reptiles, fish, or amphibians.

22. (Amended) The method of claim [21]20, wherein the amino acid sequence administered to a patient in need thereof comprises the extracellular domain of the amino acid sequence comprising SEQ ID NO: 4.

23. (Amended) The method of claim [21]20, wherein the amino acid sequence administered to a patient in need thereof comprises the intracellular domain of the amino acid sequence comprising SEQ ID NO: 4.

25. (Amended) The method of claim [25]24, wherein the patient is livestock, primates, humans, canines, felines, rodents, birds, reptiles, fish, or amphibians.

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Marked-up Claims

28. (Amended) The method of claim [28]27, wherein the screening involves performing a haplotype analysis using the nucleic acid sequence comprising SEQ ID NO: 2 and determining whether the subject contains the *Zmax1* gene or lacks an HBM polymorphism.

31. (Amended) The method of claim [31]30, wherein the tissue is liver.

32. (Amended) The method of claim [31]30, wherein the promoter that directs expression in tissue is an osteocalcin promoter or an AML-3 promoter.

34. (Amended) The method of claim [34]33, wherein the HBM protein comprises SEQ ID NO: 4.

35. (Amended) The method of claim [34]33, wherein the lipid modulated is selected from the group consisting of: VLDL, LDL, IDL, HDL, LIPOa, APO A-1, APO B and APO E.

37. (Amended) The method of claim [37]36, wherein the lipid modulated is selected from the group consisting of: VLDL, LDL, IDL, HDL, LIPOa, APO A-1, APO B and APO E.

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Marked-up Claims

38. (Amended) The method of claim [37]36, wherein the regulation of HBM or Zmax1 activity is modulates gene transcription, protein translation or Zmax1 or HBM protein binding to its cognate target thereby regulating lipid levels.

40. (Amended) The composition of claim [40]39, wherein the lipoprotein modulating agent is blofibrate, gemfibrozil, nicotinic acid, cholestyramine, cholestipol, lovastatin, simvastatin, pravastatin, probucol, premarin or estradiol.

41. (Amended) The composition of claim [40]39, wherein the lipoprotein modulating agent modulates LDL levels.

42. (Amended) The composition of claim [42]41, wherein the lipoprotein modulating agent is selected from the group consisting of bile acid binding resins, HMG-CoA reductase inhibitors and estrogens.

43. (Amended) A method of treating a subject suffering from a lipid-mediated condition comprising the step of administering the composition of claim [40]39.

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Marked-up Claims

44. (Amended) The method of claim [44]43, wherein the lipid-mediated condition is atherosclerosis, arteriosclerosis, or a disease associated with atherosclerosis or arteriosclerosis.

46. (Amended) The combination therapy of claim [46]45, wherein the agent regulating lipoprotein concentrations is blofibrate, gemfibrozil, nicotinic acid, cholestyramine, cholestipol, lovastatin, simvastatin, pravastain, probucol, premarin or estradiol.

47. (Amended) The method of claim [46]45, wherein the lipid-mediated disease is atherosclerosis, arteriosclerosis, an atherosclerosis associated condition or an arteriosclerosis associated condition.